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10/573,601	08/11/2006	Hans-Arne Hansson	1003301-000258	6872

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/573,601	HANSSON ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,16 and 20-42* is/are pending in the application.

4a) Of the above claim(s) *3-5,16,20-22 and 36-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-35,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/24/06;8/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendices A-B*.

DETAILED ACTION

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. The amendment of 22 September 2008 has been entered in full. Applicant's response to the Miscellaneous communication dated 22 August 2008, providing the corrected sequence listing and amending the claims to recite the correct SEQ ID NOs. has been acknowledged and entered. Claims 20, 21, 23 and 24 have been amended.

Election with traverse

2. Applicant's election with traverse of Group IV, claims 23-35, and 41-42 in the reply filed on 22 September 2008 is acknowledged.

3. The traversal is on the ground(s) that the inventions of Groups I-VI are closely related and a proper search of the claims of one group "should, by necessity, require a proper search of the others". Specifically Applicant asserts that because all the claims can be searched simultaneously, the present restriction requirement might lead to duplicative search and inconsistent results. Applicants further argue that the current requirement will result in a number of related applications with the same disclosure, having "the same search by different Examiners on different occasions", that may be burdensome to the PTO. Applicants emphasize that

"regardless of whether the six groups are independent or distinct", "Examiner need not have restricted the application", because based on MPEP guidelines, the entire application should be searched if no serious search burden is present, therefore, "it is not mandatory to make a restriction requirement in all situations". Applicant requests the restriction to be withdrawn.

4. Applicant arguments are fully considered, however, are not found persuasive because Groups I-VI are restricted properly as they comprise patentably distinct methods that constitute patentably distinct inventions for reasons explained in the previous Office Action dated 5 May 2008. Although the inventive groups are largely directed to methods using an antisecretory protein, Groups I-VI are directed to in vivo and in vitro methods that are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps and goals. that are distinct both physically and functionally, and are not required one for the other. For example, Group I requires the treating and preventing of a condition by administering an antisecretory secretory protein (ASP) inducing food, which is not required by the other methods. Group II requires the formation of ASP by administering malted cereal that is not required by the other methods. Group III requires in vitro maintenance of the isolated stem cell progeny by treating the cells with ASP, which is not required by the other methods. Group IV requires treating and preventing

by administration of ASP, which is not required by the other methods. Group V requires treating a patient with ASP, isolating and propagating the stem cell in vitro, and transplanting the cells to the same or another patient, which is not required by any of the other methods. Group VI requires isolating, and maintaining the genesis of isolated stem cells from the germinal layer of a patient, treating and propagating the cells with ASP (Formula I) in vitro, transplanting the cells in the same or a different patient, a process that is not required by any of the other methods. Because of the distinct objective requiring a distinct protocol for each of the above Groups, a search and examination of all six methods in one patent application would result in an undue burden, since the searches for the six methods are not co-extensive, the classification is different, and the subject matter is divergent.

5. Furthermore, pursuant to 37 C.F.R. § 1.475 (a), Unity of invention before the International Searching Authority, an international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. Groups I-VI do not possess the same or corresponding technical features as stated in the previous Office Action (page 3) and reiterated

above. Note that PCT Rule 13 does not provide for multiple products or methods within a single application.

6. **The requirement is still deemed proper and is therefore made FINAL.**

7. Claims 3-5,16, 20-22, and 36-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 22 September 2008.

8. Claims 23-35, 41-42, drawn to a method of treatment or prevention of a condition associated with a gain or loss of nervous tissue, comprising administering an effective amount of an antisecretory protein or an oligopeptide or derivative, thereof, comprising Formula I, are being considered for examination in the instant application.

9. Applicants election of species "loss of nervous tissue", "caused by damage to the central nervous system (CNS)", "axonal damage caused by head trauma", in the reply filed on 22 September 2008 is acknowledged. Applicant's non-election of species D is accepted as appropriate.

Information Disclosure Statement

10. The information disclosure statements filed 24 March 2006 and 11 August 2006 have been acknowledged and entered in full.

11. Two references on IDS dated 11 August 2006 were crossed off because these were duplicated, for being cited in the IDS dated 24 March 2006.

Claim Rejections - 35 USC § 112-Second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 23-35 and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 23 is indefinite and unclear for reciting "Formula I; SEQ ID NOS:3-6" in parenthesis next to the peptide sequence "X1-V-C-X2-X3-K-X4-R-X5". The claim recites that X1 is amino acids 1-35 of SEQ ID NO: 1 or is absent, while X5 is one of the fragments selected from SEQ ID NOS: 3-6 (SEQ ID NOs: 3-6 correspond to amino acids 43-163 - see page 6 of claim 23; also see amendments to the specification dated 3/24/06). Based on the definitions of X1 and X5 as stated above, it is not ascertainable as to how SEQ ID NOs: 3-6 can define the sequence of Formula 1. Clarification is sought for this contradiction.

14. Claim 23 is vague and indefinite for reciting Formula "**I**", wherein X1 is "**I**" (emphasis added on **I**). It is not clear as to what "**I**" stands for. Is it a Roman number "I", or is it the alphabet "**I**" for amino acid "isoleucine".

15. Claim 23 is also vague and unclear for reciting "condition **associated** with or **characterized** by…". The difference between "associated" and "characterized" is not ascertainable and is not explained in the instant specification.

16. Claim 23 is indefinite for reciting "an" antisecretory protein, meaning **any** antisecretory protein. It is unclear as to which other antisecretory protein the claims are referring to. Likewise, claim 41 recites "antisecretory factor**s**". It is not clear which other antisecretory factors the claim is referring to. The claims fail to identify the metes and bounds of the related subject matter.

17. Claims 24-35 and 41-42 are rejected for depending from the indefinite claim 23.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 23-35 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment by increasing neuronal proliferation comprising administering Formula I comprising the active N-terminal region of ASP comprising 1-163 amino acids or certain fragments thereof (e.g. amino acids 36-51)

Which ones, specifically?

for conditions associated with a pathological loss of nervous cells or tissue or memory loss, such as head trauma, Alzheimer's Disease or cerebral hemorrhage in rats or mice, does not reasonably enable for the treatment of the claimed conditions in a patient by the administration of any oligo polypeptide or derivatives of Formula I as broadly claimed in claims 23 and 24. The specification also does not enable a method of prevention of any of the claimed conditions by administration of the claimed peptides to a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

19. The claims are directed to a method for treating or preventing a condition associated with a pathological loss of nervous tissue comprising administering to the patient an antisecretory protein, or an oligopeptide or derivatives thereof comprising an amino acid sequence of Formula I (claims 23, 24 and 35). The claims further recite that the condition is characterized by a loss of control of regeneration, loss of cells in the CNS,

comprising neural stem cells, oligodendroglia and cholinergic neuronal cells, etc. (claims 25-29). Still further the claims recite that the condition is caused by damage to the CNS such as a head trauma, and is further characterized by memory loss (claims 30-34). Finally, the claims recite that the conditions are associated with an insufficient formation of antisecretory factors and an insufficient function of AF receptors (claims 41-42). It is noted that the Examiner has broadly interpreted the phrase "an antisecretory protein" and "antisecretory factors" (claims 23, 41) to encompass any antisecretory protein or factor, and oligopeptides or fragments thereof.

20. With respect to claim breadth, the standard under 35 U.S.C. § 112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification (see MPEP 2111 [R-1]), which states that claims must be given their broadest reasonable interpretation.

21. "During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." *In re Hyatt,* 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner

reduces the possibility that the claim, once issued, will be interpreted more broadly that is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)".

22. As such, the broadest reasonable interpretation of the claimed method is for treatment and/or prevention of any condition associated with a loss of any nervous tissue or cells, comprising administration of an ASP, comprising Formula I, or any oligopeptide or derivative thereof to a patient.

23. The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands,* 8 USPQ2d, 1400 (CAFC 1988).

24. The specification of the instant application teaches that ASP is a 41kD natural protein secreted from the pituitary gland, and comprising 382 amino acids. The specification also teaches that the active site of ASP for anti-inflammatory and antisecretory effects is located in the N-terminal regions of ASP having residues 1-163, such as amino acids 36-52 (page 4, lines 9, 10, 15-20). Still further the specification teaches that ASP is homolgous to S5a or Rpn10, a subunit of the 26S proteasome (page 4, lines 23-25). The specification teaches that certain fragments of ASP can repair or regenerate nervous tissue components and reduce the rate and

extent of degeneration and tissue destruction, thereby providing improved methods for treating injuries and disorders of the CNS (page 5, lines 23-25). Using the freezing probe in the rat model for brain injury, the instant specification demonstrates increased proliferation of neural stem cells and neural progenitor cells in the subgranular zone (SGZ) of the hippocampus in rats fed with an enriched SPC diet to induce the formation of ASP, along with reduced gliosis, brain edema, reduced formation of amyloid, etc. (Examples 3, 4; figure 3). Example 5 demonstrates that rats receiving intravenous injection of a 16 amino acid fragment of ASP comprising amino acids 36-51 subsequent to freezing brain injury, also results in increased proliferation of neuronal cells in the SGZ and the subventricular zone (SVZ). However, the specification does not disclose the administration of any fragment, oligopeptide or derivative of Formula I or amino acids 1-163 of SEQ ID NO: 1 to be used for treating the claimed conditions. The specification also does not teach the specific polypeptide domains of formula I or ASP necessary for preserving the biological activity, in this case increasing neuronal cell proliferation for conditions displaying a loss in nervous tissue. Furthermore, the specification does not teach functional or structural characteristics of all oligopeptides and derivatives of Formula I encompassed in the claims other than the ASP polypeptide comprising the full-length active domain of amino acids 1-163 or "certain" fragments thereof, e.g. amino acids 36-51.

25. Relevant literature teaches that antisecretory factor or ASP, a protein known to inhibit the intestinal fluid secretion induced by cholera toxin, and isolated from the anterior pituitary gland, is transported to the gut with the blood (Johansson et al. JBC 270: 20615-20620, 1995; abstract; col 2, para 1; page 20617), and has a peptide sequence that is 100% homologous to Formula I of the instant claims (see SCORE alignment on Appendix B). The literature further teaches that another homologous peptide, presenilin interacting protein, also called antisecretory factor, and having a sequence homology with the instant Formula I can be used as a therapeutic and a diagnostic for neurodegenerative and neurotraumatic disorders like AD and cerebral hemorrhage ((St. George-Hyslop et al., (International Application Publication No. WO 97/27296, dated 31 July 1997), abstract; pages 96-98; page 5, line 20 - page 6, line 2; page 7, lines 1-9). The prior art also teaches that an enriched environment can result in the formation of more hippocampal neurons in adult mice (Kempermann et al. Nature 386: 493-495, 1997). However, it is not even clear from the relevant literature as to what regions of the ASP sequences or the maximum length of the sequences are essential for the claimed biological activity. It also not clear as to what regions of ASP are particularly formed after feeding rats or mice with enriched diet, or as in the instant case with SPC diet. Also unclear is how specific the effect of ASP is, when feeding rats on an enriched diet, especially considering as Kempermann et al. states “factors

still unknown, contribute to the enhanced performance induced by exposure to an enriched environment" (page 495, para 1). Thus, undue experimentation would be required of the skilled artisan to identify the precise structural characteristics of the claimed Formula I, or oligos or derivatives thereof having the therapeutic effect in conditions characterized by loss of neuronal cells or tissues.

26. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the

antisecretory protein or Formula I which are tolerant to change (e.g. such as by amino acid substitutions or deletions or modifications), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

27. Furthermore, the term 'prevention' (recited in the claims) corresponds to stopping of conditions associated with loss of nervous tissue by administration of ASP or Formula I. The instant examples in the specification indicate increased neuronal proliferation after the induction of ASP formation (via enriched diet), or following the administration of a 16 mer oligo peptide of Formula I or SEQ ID NO: 1, subsequent to freezing injury in rats. It is noted that the results depict a decreased tissue loss, not an injury induced **zero tissue loss** following ASP treatment, as would have been expected had there been prevention (emphasis added). The

instant claims and the specification merely indicate neuroprotection from a greater tissue loss, however, does not indicate a preventive or prophylactic measure. Undue experimentation would thus be required of the skilled artisan to establish the onset of nervous tissue loss and administer the effective oligos or derivatives of ASP or Formula I to prevent the CNS tissue or cell degeneration.

28. Additionally, it cannot be concluded with certainty that a "greater number of neurons in the dentate gyrus leads to enhanced behavioral performance" (Kempermann et al., page 495, last para). Since the treatment of a condition in a patient would entail physiological and functional improvement, the instant specification fails to provide adequate guidance to the skilled artisan to make and use the full scope of the inventive method, resulting in undue experimentation to use any oligopeptide or derivative of Formula I for treating the condition in totality.

29. Due to the large quantity of experimentation necessary to generate the infinite number of ASP or Formula I oligos or derivatives recited in the claims and possibly screen the same for treatment or prevention of conditions characterized by CNS tissue loss; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims

which fail to recite any structural or functional limitations and also encompass a broad class of oligos and derivatives - undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, first paragraph- Written Description

30. Claims 23-35 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

31. The claims are directed to a method for treating or preventing a condition associated with a pathological loss of nervous tissue comprising administering to the patient an antisecretory protein, or an oligopeptide or derivatives thereof comprising an amino acid sequence of Formula I (claims 23, 24 and 35). The claims further recite that the condition is characterized by a loss of control of regeneration, loss of cells in the CNS, comprising neural stem cells, oligodendroglia and cholinergic neuronal cells, etc. (claims 25-29). Still further the claims recite that the condition is caused by damage to the CNS such as a head trauma, and is further characterized by memory loss (claims 30-34). Finally, the claims recite

that the conditions are associated with an insufficient formation of antisecretory factors and an insufficient function of AF receptors (claims 41-42). It is noted that the Examiner has broadly interpreted the phrase "an antisecretory protein" and "antisecretory factors" (claims 23, 41) to encompass any antisecretory protein or factor, and oligopeptides or fragments thereof.

32. The specification of the instant application teaches that ASP is a 41kD natural protein secreted from the pituitary gland, and comprising 382 amino acids. The specification also teaches that the active site of ASP for anti-inflammatory and antisecretory effects is located in the N-terminal regions of ASP having residues 1-163, such as amino acids 36-52 (page 4, lines 9, 10, 15-20). Still further the specification teaches that ASP is homolgous to S5a or Rpn10, a subunit of the 26S proteasome (page 4, lines 23-25). The specification teaches that certain fragments of ASP can repair or regenerate nervous tissue components and reduce the rate and extent of degeneration and tissue destruction, thereby providing improved methods for treating injuries and disorders of the CNS (page 5, lines 23-25). Using the freezing probe in the rat model for brain injury, the instant specification demonstrates increased proliferation of neural stem cells and neural progenitor cells in the subgranular zone (SGZ) of the hippocampus in rats fed with an enriched SPC diet to induce the formation of ASP, along with reduced gliosis, brain edema, reduced formation of amyloid, etc. (Examples 3, 4; figure 3). Example 5 demonstrates that rats receiving

intravenous injection of a 16 amino acid fragment of ASP comprising amino acids 36-51 subsequent to freezing brain injury, also results in increased proliferation of neuronal cells in the SGZ and the subventricular zone (SVZ). However, the specification does not teach functional or structural characteristics of all encompassed ASP or Formula I polypeptide, oligos and derivatives. The brief description in the specification of one ASP polypeptide (SEQ ID NO: 1), one N-terminal active region comprising Formula I (amino acids 1-163 amino acids of SEQ ID NO: 1), and one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all oligopeptides and derivatives of ASP or Formula I or SEQ ID NO: 1. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. However, in this case, the specification has not shown a relationship between the structure, function, or properties of the claimed genus of polypeptides. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the

specification does not provide adequate written description of the claimed genus.

33. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

34. With the exception of the ASP polypeptide (SEQ ID NO: 1), one N-terminal active region comprising Formula I (amino acids 1-163 amino acids), and one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or production. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The *polypeptide itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

35. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to

mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

36. Therefore, only ASP polypeptide (SEQ ID NO: 1), one N-terminal active region of Formula I (comprising amino acids 1-163 amino acids), one ASP oligo (amino acids 35-51 of SEQ ID NO: 1), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

37. Claims 23-35, and 41-42 are rejected under 35 U.S.C. 102(b) as clearly anticipated by St. George-Hyslop et al., (International Application Publication No. WO 97/27296, dated 31 July 1997), as evidenced by

Barten et al. (Mol Neurobiol. 37: 171-186, 2008) and Roth et al. (Biol Res 38: 381-387, 2005).

38. The claims are directed to a method for treating or preventing a condition associated with a pathological loss of nervous tissue comprising administering to the patient an antisecretory protein, or an oligopeptide or derivatives thereof comprising an amino acid sequence of Formula I (claims 23, 24 and 35). The claims further recite that the condition is characterized by a loss of control of regeneration, loss of cells in the CNS, comprising neural stem cells, oligodendroglia and cholinergic neuronal cells, etc. (claims 25-29). Still further the claims recite that the condition is caused by damage to the CNS such as a head trauma, and is further characterized by memory loss (claims 30-34). Finally, the claims recite that the conditions are associated with an insufficient formation of antisecretory factors and an insufficient function of AF receptors (claims 41-42).

39. St. George-Hyslop et al. teach that presenilin-interacting protein of SEQ ID NO: 2, also known as antisecretory factor and the multiubiquitin chain binding S5a (page 15, lines 8-10) comprises a sequence that is 100% homologous to Formula I comprising amino acids 1-163 of SEQ ID NO: 1 (see SCORE alignment in Appendix A) that can be used as therapeutics for the treatment of Alzheimer's Disease (AD) and other related disorders having abnormalities in this protein, e.g. cerebral

hemorrhage (abstract; pages 96-98; page 5, line 20 - page 6, line 2; page 7, lines 1-9), by administering the protein to the affected brain (page 75, lines 17-20). The reference further teaches that the protein can be administered parenterally as a pharmaceutical preparation or vaccine either by subcutaneous or intramuscular injection (page 78, lines 1-2). Because AD and other related disorders arise due to abnormality of the protein, it would inherently indicate an insufficient formation of the antisecretory factor and/or insufficient function of the protein receptors or other binding constituents. It is well-known that AD and related degenerative disorders like cerebral hemorrhage are associated with loss of nervous tissue, loss of control of regeneration and a loss of cells in the CNS. It is further inherent that cerebral hemorrhage or AD can be caused by traumatic brain damage and further lead to memory loss. Additionally, AD is known to be caused by a loss of cholinergic neurons and is further associated with loss of oligodendrocytes as evidenced by Barten et al. (page 176, col 2, para 1), and Roth et al. (abstract). Therefore, the reference anticipates the claimed invention.

Conclusion

40. No claims are allowed.

41. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose

telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

42. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

43. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
15 December 2008

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649